



POSTER PRESENTATION

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# Lack of adalimumab's complement dependent cytotoxicity on human cells expressing complement regulatory proteins

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## Introduction

It has been reported that upon binding to membrane TNF (mTNF), adalimumab may activate the complement system, leading to complement dependent cytotoxicity (CDC) of targeted cells. CDC has been implicated in mechanisms of action conferring adalimumab's efficacy. CDC has also been proposed to contribute to the reactivation of opportunistic infections. CDC attributed to adalimumab in the U.S. product label refers to a mouse cell line transfected with a non-cleavable form of human TNF (SP2/0-11A5).

## Aim

The objective of this preclinical study was to assess the CDC activity of adalimumab in four different cell populations expressing human TNF: 1) mTNF-transduced human MonoMax-6 (MM6); 2) LPS-activated human acute monocytic leukemia cell line (THP-1); 3) LPS-activated human peripheral blood mononuclear cells (PBMC) from normal and Rheumatoid arthritis (RA) donors; and 4) mTNF-expressing, murine myeloma SP2/0-11A5. We also determined surface expression of complement regulatory proteins and adalimumab binding on these cells.

## Methods

Calcein-labeled cells were cultured with test antibodies plus complement and released calcein from dying cells was measured to assess CDC. Expression of mTNF and complement regulatory protein expression was measured by flow cytometry.

## Results

Adalimumab was not associated with CDC of mTNF-MM6, LPS-activated THP-1, normal PBMC or RA PBMC. As previously reported, adalimumab was associated with CDC of human TNF transfected murine SP2/0-11A5-1 cells. Adalimumab was shown to bind to TNF expressed on the surface of activated human PBMC or THP-1 cell lines, and also to non-cleavable mutant forms of mTNF expressed on human or mouse cell lines. Expression of complement regulatory proteins was observed for all human cells, but was absent from mTNF-transfected mouse cell line, Sp2/0-11A5.

## Conclusions

Adalimumab was not associated with CDC reactions and the death of human cells from healthy volunteers or RA patients nor human cells lines. The expression of complement regulatory proteins by the human cells may account for the difference from the data reported for transfected murine SP2/0-11A5-1 cells.

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